Ontario

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MacLEOD (cont'd)

ROYAL COMMISSION OF INQUIRY INTO CERTAIN DEATHS AT THE HOSPITAL FOR SICK CHILDREN AND RELATED MATTERS.

Hearing held
8th floor
180 Dundas Street West
Toronto, Ontario

X Young
Labaw
Risley
Roland

The Honourable Mr. Justice S.G.M. Grange	Commissioner
P.S.A. Lamek, Q.C.	Counsel
E.A. Cronk	Associate Counsel
Thomas Millar	Administrator

Transcript of evidence
for

November 21, 1983

Re: Sr. PMC

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ROYAL COMMISSION OF INQUIRY INTO CERTAIN DEATHS AT THE HOSPITAL FOR SICK CHILDREN AND RELATED MATTERS.

Hearing held on the 8th Floor, 180 Dundas Street West, Toronto, Ontario, on Monday, the 21st day of November, 1983.

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THE HONOURABLE MR. JUSTICE S.G.M. GRANGE - Commissioner

THOMAS MILLAR - Administrator

MURRAY R. ELLIOT - Registrar

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APPEARANCES:

P.S.A. LAMEK	Commission Counsel
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I. J. ROLAND) M. THOMSON)	Counsel for The Hospital for Sick Children
D. YOUNG	Counsel for The Metropolitan Toronto Police
W.N. ORTVED	Counsel for numerous Doctors at The Hospital for Sick Children
F. KITELY	Counsel for the Registered Nurses' Association of Ontario and 35 Registered Nurses at The Hosiptal for Sick Children

(Cont'd)

APPEARANCES: (Continued)

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E. FORSTER	Counsel for Phyllis Trayner - Nurse
J. A. OLAH	Counsel for Janet Brownless - R.N.A.
B. KNAZAN	Counsel for Mrs. M. Christie - R.N.A.
S. LABOW	Counsel for Mr. & Mrs. Gosselin, Mr. & Mrs. Gionas, Mr. & Mrs. Inwood, Mr. & Mrs. Turner, Mr. & Mrs. Lutes, and Mr. & Mrs. Murphy (parents of deceased children)
F.J. SHANAHAN	Counsel for Mr. & Mrs. Dominic Lombardo (parents of deceased child Stephanie Lombardo); and Heather Dawson (mother of deceased child Amber Dawson)
J. SHINEHOFT	Counsel for Lorie Pacsai and Kevin Garnet (parents of deceased child Kevin Pacsai)

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---Upon comencing at 10:30 a.m.

DR. STUART MAXWELL MacLEOD, Recalled

THE COMMISSIONER: Mr. Olah, had you finished? You had finished your cross-examination or had you not?

MR. OLAH: Yes, I had.

THE COMMISSIONER: All right. Thank you.

MR. OLAH: Thank you.

THE COMMISSIONER: Mr. Young, I think we skipped you over at your request, did we not?

MR. YOUNG: Yes, you did.

THE COMMISSIONER: Do you still want to be skipped?

MR. YOUNG: No, I have a few questions I would appreciate putting to the witness now.

THE COMMISSIONER: Yes. All right. Yes, if you will do that now then, Mr. Young.

MR. YOUNG: Before I do, Mr. Commissioner, on November 10th when Dr. MacLeod was here last Mr. Lamek was examining him, there was some discussion of a computer printout dealing with Baby Pacsai.

There is mention of it at page 4262 and I believe on the previous page. I understand there had earlier been a suggestion made that the police had obtained various materials from the Hospital including this particular computer printout.

We have searched for the printout and discussed it with the officers involved, and they do not recall any such printout being seized. The only documents they had were the documents that are now in the Pacsai chart.

I'm afraid we can't be of any further assistance but I thought I would let you know.

THE COMMISSIONER: All right.

CROSS-EXAMINATION BY MR. YOUNG:

Q. Doctor, my name is David Young and as you have probably figured out by now I am one of the counsel representing the Metropolitan Toronto Police.

I just have a few questions for you on one point: we spent quite a bit of time over the last couple of weeks or I guess two weeks now trying to determine when Baby Cook would likely have been administered that last dose of digoxin. I believe you told us that the earliest time was probably at about 3:45.

Is that right?

A. Yes.

Q. You have also told us that - I think you told us in answer to a question put to you by Miss Forster that a baby the size of Justin Cook just couldn't handle a certain volume of liquid put into him. For instance, it is unlikely that he could handle 30, 40 adult volumes of digoxin. It would just be physically impossible to inject that into the child. Is that right?

A. I don't recall that discussion but I think that is correct.

Q. All right. It wouldn't be, though, Doctor, impossible to inject two adult vials into a child?

A. No, there would be no trouble.

Q. Now, you also discussed two weeks ago, Doctor, the problems that would arise from trying to administer 40 vials to this particular infant as has been suggested at various times. You said there would be a lot of mess, a lot of broken glass and a great deal of time spent doing that. Is that right?

A. Yes, I believe we talked about the logistical difficulties of opening and drawing up all of these vials. I don't recall specifically

talking about the problems of volume administered to infants of this size although I think that has been gone over.

Q. Well, as long as we can agree on it I can get that reference but that is fine, Doctor.

Doctor, my only point is that it seems to me that there is a lot of middle ground that if there was more than one vial we don't have to be talking about 40 vials.

For instance, two vials, two adult vials of digoxin, if indeed that was administered to Baby Cook, that would move the time of administration back to an earlier time than 3:45; is that correct?

A. Perhaps a little bit, yes. I think there are other - there were other factors, though, that went into the discussion about time. It is true that you can change the times slightly by postulating different amounts of drug administerd.

MR. YOUNG: That is my only point. Thank you very much, Doctor.

THE COMMISSIONER: Miss Kitely, did we pass you by last time?

MS. KITELY: You passed me by at my request, sir, and I am waiting for something to

be copied and to be deliverd.

THE COMMISSIONER: All right.

MS. KITELY: I wonder if Mr. Labow might continue?

THE COMMISSIONER: Yes. All right.

Mr. Labow?

CROSS-EXAMINATION BY MR. LABOW:

Q. Doctor, my name is Steven Labow and I represent among others the parents of Kristin Inwood. My questions will be mainly directed to the Inwood child.

Before I get into that, Doctor, you mentioned that digoxin toxicity is a diagnosis of exclusion.

A. Yes, I think I said that.

Q. Is that true with all drug toxicity?

A. No, I don't think you can generalize to all drugs. There are some agents that have very specific types of toxicity.

In the case of digoxin the toxic manifestations are relatively non-specific considering that the patients who are likely to receive digoxin already have cardiac disease, so they may have any of the cardiac manifestations of digitalis toxicity

simply on the basis of their cardiac disease.

Q. Are there many other toxic drugs - I am dealing specifically with children with cardiac disease - that would fall into that category of being a diagnosis of exclusion.

A. I think - I am not sure I follow your question exactly, but I think that most cardiac drugs given to patients with cardiac disease would present great difficulties in identifying cardiac toxicity so that virtually none of them have very specific cardio toxicity at least in the acute case; that is shortly after administration of the drug.

Q. Thank you.

Now notwithstanding that digoxin toxicity is that kind of diagnosis, if there is a digoxin assay done either just prior to death or just after death, would that help persuade you one way or the other?

A. Well, this is one of the reasons for doing digitalis assays in blood is to try to distinguish between abnormal cardiac performance secondary to disease and abnormal performance secondary to the drug: in this case digoxin. So, yes, surely your opinion would be influenced by the

concentration measurement.

Q. Now, Doctor, regarding Kristin Inwood you pointed out it was her case more than any other that made you re-examine some of your pre-suppositions.

A. Yes.

Q. Of many of the other cases. What pre-suppositions were you working on that you looked into?

A. Well the - I think at the time of the initial investigation and at the time certainly right up to the time of the preliminary hearing a lot of the testimony, and I am referring particularly to Dr. Hastreiter's testimony, a lot of that was based on the assumption that concentrations were measured at what we call steady state. That is we were beyond this alpha phase of distribution. And when we saw this concentration of I believe it is 491 nanograms per ml in Kristin Inwood it was clear that that couldn't be a steady state concentration.

I don't think it is - well, nothing is impossible but that really would be at the outer fringe of possibility for somebody to survive long enough to have that kind of a steady state concentration of digoxin.

It would also require, and this is I believe what came out at the preliminary hearing, it would require a supposition of administration of really immense amounts of digoxin in order to achieve that concentration at steady state. And that is where you get into the question of whether it is really logistically possible to administer 30 or 40 vials of digoxin to a small baby.

Because of all of these things we felt you had to assume in Inwood's case if that value was correct that it represented a distribution measurement, an alpha phase measurement.

Q. Now regarding the Inwood sample you and most other people who discussed it have concerns about what the sample went through and how it was treated and how that may affect the reading.

A. Yes. I think that is correct. I have to point out that I don't know a great deal firsthand about how it was handled. Certainly I haven't seen Mr. Cimbura's records and none of the people who work with me have seen them.

Q. Now one of the big concerns seems to be, though, that it was heated and the heating and the cooling might affect the digoxin levels in the sample.

A. Yes, that is correct.

Q. Do you have any scientific basis for that suspicion?

A. Well, I think you would certainly anticipate on the basis of release of digoxin from red blood cells that that sort of treatment would change the concentration; would change the serum concentration of the plasma concentration, and we know that in babies of this age the concentration of digoxin in red blood cells is approximately three times as high as it is in plasma. So the heating and cooling and handling of that sample, if it was whole blood, would cause an elevation of the plasma digoxin.

Now I am not sure in fact that it was whole blood at the time it was heated.

Q. My understanding is that it was serum.

A. I think it may already have been serum.

Q. If it was serum.

A. If it was serum then I don't think that the heating and cooling per se would change the concentration.

Q. Now another of your concerns

is that you would like to know whether or not this was very specifically digoxin.

A. Yes.

Q. In that sample.

A. Yes, that is correct.

Q. Is that correct?

A. Again this relates to the heating and cooling phenomena. The other possibility is that there is something in heating or in this kind of physical manhandling of the sample that may release digoxinlike substances from other proteins or might even cause creation de novo of substances which interfere with the assay.

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Q. Well, this assay was done, according to Mr. Cimbura, by RIA AND HPLC and RIA?

A. Yes.

Q. Do you have a real concern that most of his finding is not digoxin?

A. Oh, I think it is - you know, I really don't want to speculate on that without seeing his data. I think it is logical for you to assume that it probably is. Certainly the HPLC RIA technique is a relatively specific assay but it is certainly not sufficiently specific to distinguish between this multitude of substances which may have digoxin-like activity and true digoxin. So, the only really specific assay here is a mass spectrographic assay.

Q. Now, the hospital does digoxin assays as a matter of course at this time?

A. Yes.

Q. What kind of assay do you use, today?

A. Today. Well, generally we use a technique called TDX, which is an automated technique which has been introduced in about the last six months.

Q. Is that more specific than

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Mr. Cimbura's assay?

A. No. No, I wouldn't say, not more specific than the HPLC/RIA technique.

Q. But the hospital is satisfied with that as a relatively accurate indication for digoxin?

A. Well, for clinical purposes it is quite adequate, so is the RIA in most cases. Mr. Cimbura's assay is more specific than this standard clinical assay. All I am suggesting is that it is not necessarily adequate for forensic purposes.

Q. Now, assuming that the 491 reading is essentially valid, you said that you could infer that there was an excessive dose of digoxin given to that child?

A. Yes. When you say essentially valid, or maybe I said essentially valid.

Q. No, I am saying essentially valid.

A. You have to take into account the potential multiplier factor, and we have been through all the uncertainties of that, so, it may be anywhere from in fact less than 1 to 10 or 15. But assuming that it is 3 or 4 then we are really

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talking about an ante mortem concentration of maybe 125 nanograms per ml and if that is a true reading then you must assume that there was an overdose of digoxin administered.

Q. Now, assuming that the multiplier was 3 or 4, would the dose given necessarily be lethal or fatal for this child?

A. Well, you can never say always in medicine or toxicology and I think when we left off the last time I had pointed out a couple of cases where there were very high serum digoxin concentrations. I think the youngest was in a 10-year old child and in spite of those high concentrations yet had not ensued and certainly there are cases of people surviving for hours with levels of 200 nanograms per ml and eventually being treated with some heroic measures leading to survival. But normally you would not expect somebody to survive with that kind of a concentration, although, I have to qualify that again to say that it depends where you are on that alpha distribution phase. If that 125, that I think I went through some mathematics on the board here two weeks ago, if that 125 is in fact the very peak of the alpha phase, the concentration just minutes or even seconds after administration, then it may not be terribly much.

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So, it is possible that that is a very misleading figure.

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THE COMMISSIONER: Do we know, doctor, what the top of the alpha phase is for a therapeutic dose for a child?

THE WITNESS: Well, it depends a little bit on the speed of administration. I think I calculated here on the board that with the Inwood case in particular that a dose of even 50, or I think the actual figure was 49 micrograms would have been enough to give that concentration.

THE COMMISSION: I am sorry, I haven't figured out what 49 micrograms is in relation to a pediatric ampoule.

THE WITNESS: Oh, that would be one pediatric ampoule. There is 50 micrograms.

THE COMMISSIONER: That would be sufficient to produce at the top of the phase.

THE WITNESS: At the very top of the alpha phase. Now, that assumes that it was given quite rapidly.

THE COMMISSIONER: What kind of a reading did you say, 50?

THE WITNESS: No, a reading of 491.

THE COMMISSIONER: Yes.

THE WITNESS: If we took that as being

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a true value. But that is assuming that it is given over a period of seconds and that the sample was taken within seconds or, at the most, a minute after that administration.

THE COMMISSIONER: If a pediatric ampoule were administered in the ordinary fashion, that is, in the therapeutic fashion?

THE WITNESS: Yes.

THE COMMISSIONER: Do we have any figures or any thoughts on how high the reading could be. It is not to be taken, as we know, six hours or something, but if it were taken five minutes after administration or five minutes, or at the highest level of the alpha phase, do you know what it would be?

THE WITNESS: Well, at the very highest level - now, I am assuming here administration over perhaps five minutes.

THE COMMISSIONER: Well, whatever the normal method is.

THE WITNESS: Yes. Well, I am not sure that it is written in stone how it should be administered but it shouldn't be administered over seconds anyway.

THE COMMISSIONER: No.

THE WITNESS: It wouldn't be unreasonable to see at the very peak a level of 200, 250 nanograms per ml. Now, I am talking about administration of a full pediatric ampoule, 50 micrograms, which wouldn't be the therapeutic dose for Kristin Inwood. But then if you get out, say, 10 minutes later or, you know, say five minutes later you might expect to be down by a third and 10 minutes later down by two-thirds. So, even within 10 minutes with one ampoule you could have a level of 100 to 125 nanograms per ml which could, given this multiplier effect, produce this reading of 491.

THE COMMISSIONER: Okay.

MR. LABOW: Q. Now, Doctor, this child arrested at approximately 2:30 and there was a very unsuccessful resuscitation effort, which you have already looked into and there was very little response, and the child was pronounced dead at 3 o'clock.

Now, would that half-hour time period,would there be much distribution in that half-hour time period?

A. Could I see the chart on Kristin Inwood?

Q. Yes, it is Exhibit 113.

A. Yes, I believe that this is the resuscitation which was characterized by little or no response and there is a note from Dr. Mounstephen there, is there not?

Q. Correct, it is on page 62.

A. Well, again, I think I said the last time you would have to put this question directly to Dr. Mounstephen but judging from his notes I would not think there was very much circulation of the drug, or very much further distribution during the resuscitation period. But again, if cardiopulmonary resuscitation is at all successful, and this doesn't, you don't have to establish heart rhythm in order to achieve some circulation of the blood, so, I think it would be misleading for me to suggest that there was no further distribution at all, but it wouldn't follow the normal pattern of distribution.

Q. Now, Doctor, this child entered the hospital on the 11th of March and digoxin was ordered 'held' and then she was given a mistaken dose. Now, she died 21½ hours after the last known dose of digoxin was given. Could we infer quite strongly that she was given digoxin some time just before she died?

A. Oh, I think provided that that reading of 491, or some version of it is confirmed, then, yes, I think you could infer that.

Q. Now, Doctor, you commented that the tissue levels in this child are compatible with reasonable therapeutic doses?

A. Yes. Well, can you just refresh my memory as to what they are?

Q. They were 230 in the left ventricle, 79 in the left atrium and 300 in the septum ?

A. Yes.

Q. And Mr. Cimbura has estimated in his report that the concentration of digoxin in heart was not less than 549 nanograms per gram?

A. Well, that is certainly an unremarkable figure in a child who is on digoxin.

Q. Does it remain unremarkable even though she wasn't supposed to receive digoxin for at least two days before her death?

A. Yes.

Q. And hadn't received it a day before her death?

A. Yes, it remains unremarkable.

Q. Mr. Cimbura found it supportive.

A. Well, I couldn't go that far.

Q. Now, Doctor, at page 4439 of the transcript - this is Volume 64 - you told Mr. Olah when he asked you about the sample that we are concerned with in Kristin Inwood's case:

"I did not make any inquiries myself. I have read reports that described how it was kept."

Whose reports did you read?

A. Well, I was referring there primarily to I believe Dr. Bain's report. You have to realize there have been so many memos and reports floating around the hospital. I can't be absolutely certain of that but I believe it is discussed in Dr. Bain's report.

Q. So, it was Dr. Bain's report, not a report that we haven't heard about.

A. Oh, no, I don't think so. I think it may also have been discussed in Dr. Kauffman's report but I am not certain of that.

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A. We spent a great deal of time discussing the analytical problems with many of these samples. So, you know, this has come up repeatedly in discussions whether or not we accept that as a valid measurement.

Q. Now, Dr. Phillips testified in Volume 59, Page 3116, that if the reading of 491 was a true reading, then that would be an over-riding factor, would override all else and a cause of death in this case would be digoxin toxicity; do you agree or disagree with that statement?

A. Well, I don't want to get back into the semantic argument. Again, it is post hoc, ergo propter hoc, I really don't think you can assume that a higher reading per se tells you that that is the cause of death. It is perfectly compatible with digoxin as a cause of death. Perhaps we caught the beginning of the alpha phase, we see a high concentration, perhaps the child was dying of other factors, the arrest, was not going to survive the arrest in any case. You cannot assume that just because of the high reading that is the cause of death, and I think Dr. Phillips would agree with that, too, if he

considered it.

Now, if this child had congenital heart disease and was given a small dose of digoxin, a pediactric ampule, larger than she should have received, not an incredibly large dose, would that have contributed to her heart failure?

A. I don't think it would contribute directly to heart failure, unless -- the only way in which it could worsen heart failure would be by causing an arryhthmia which disrupted the heart's ability to pump her blood, and that could happen, of course, but you know, that requires a little speculation. Normally speaking we wouldn't think of digoxin as worsening heart failure.

Q. So it wouldn't worsen the heart failure, but it could contribute to causing some kind of arrhythmia?

A. Yes, that is correct.

MR. LABOW: I have no further questions.

THE COMMISSIONER: Thank you, Mr. Labow. Are you ready now, Miss Kitely?

MS. KITELY: Yes, Mr. Commissioner.

CROSS-EXAMINATION BY MS. KITELY:

Q. Doctor, my name is Kitely and I act for the Registered Nurses Association of Ontario, and some of the individual nurses, other than those that are separately represented at this hearing.

I gather from your evidence and your c.v. that you are Chairman of the Pharmacy and Therapeutic Committee.

A. At the hospital, yes, that is correct.

Q. And are you still in that capacity today?

A. Yes, I am.

Q. And were you between July, 1980 and March, 1981?

A. July, 1980, yes, I was.

Q. And am I correct as a result of your chairmanship of that Committee you have something to do with the Pharmacy Department?

A. Yes.

Q. You have some interaction with the Department?

A. Yes, that is correct.

Q. You are clearly not head of the Department but obviously you are involved

with the operation of the Department?

A. Well, that Committee represents the wishes of the medical staff to the pharmacy, and in return represents the concerns of the Pharmacy Department to the Medical Advisory Committee and to the administration.

Q. Do nursing concerns figure into that Committee?

A. Well, I can answer that two ways. At that time -- there certainly is representation from the Department of Nursing on the Committee and has been as long as I have been there. At that time that was the limit of the contact between nursing and the pharmacy on a formal basis. Since 1981, or since mid-1981 there has been a nursing Pharmacy Committee which meets regularly, where a number of issues of mutual concern are discussed and sometimes matters arising out of those meetings are brought back to the Pharmacy and Therapeutics Committee for some decision, some administrative action, various things have changed a little bit. Certainly even in 1980 there was a place where the Department of Nursing could raise issues concerning pharmacy.

Q. I understand in response,

I think, to Mr. Hunt's questions about whether or not 40 vials was possible, that you said, even given the relatively inadequate drug distribution system we had in 1981, that the loss of 40 vials would be noticed by the Pharmacy Department, do you recall that?

A. Yes, I recall that.

Q. So you would agree with me that during the period, the time we are discussing, namely, July 1980 to March, 1981, the drug distribution system in the hospital left somewhat to be desired.

A. Oh, yes, I think that would be generally agreed on.

Q. A great deal to be desired?

A. Yes, I will give you a great deal to be desired.

Q. In fact, Doctor, the Pharmacy Department, or the drug distribution system in the hospital, to put it more appropriately, was under study on several occasions in the last five years?

A. Five years prior to that time?

Q. No, in the last five years.

A. Well, there have been concerns about the pharmacy and I am aware of one

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indepth study.

Q. Which one are you aware of, Doctor?

A. Well the one that was carried out after I became the Chairman of the Pharmacy and Therapeutics Committee which was the Summers, where you probably know it as the Summers/Dinel Report.

Q. That was after you got on the Pharmacy Committee?

A. Yes, that is correct.

Q. The document I have given you, Doctor, is called the "Review of Pharmacy Services, The Hospital for Sick Children", and it has a date July 30th to August 1st, 1980, this is the Dinel and Summers Report to which you have just referred?

A. Yes, that is correct.

MS. KITELY: Mr. Commissioner, may I ask that that be marked as the next exhibit?

THE COMMISSIONER: Yes, all right, Exhibit 257.

---EXHIBIT NO. 257: Review of Pharmacy Services, The Hospital for Sick Children, Toronto, 30th July - 1 August 1980 by Brian Dinel and Jack L. Sommers.

MS. KITELY: Q. Now, this is the

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one that was prepared for the administration of the Hospital, and I gather it was after you became Chairman of the Committee?

A. Yes, this review was prepared really at the request of the Medical Advisory Committee, on request of the Pharmacy and Therapeutics Committee.

Q. So, did you take some initiative in having this report prepared, Doctor?

A. Yes, I did.

Q. Can I deal with a couple of things in this report? First of all if you will look at the Terms of Reference, the third item after "Terms of Reference" was "Review of Drug Distribution Services to In-Patient Areas".

A. Yes.

Q. That was an area of some great concern to your Committee?

A. Yes, it was.

Q. And the recommendations in connection with that concern are found on page 2, and under "Summary of Recommendations" I am directing your attention to (B) being the Medication System, is that correct, Doctor?

A. Yes.

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Q. So those concerns, or those recommendations listed as 5, 6, 7, 8, 9 refer to the drug distribution services concern on the previous page.

A. Yes. I am not sure that they directly address the other concerns. Well, I guess the first one is so general that it does. The others are referring to specific problems with drug distribution, the hours of service in the Hospital which had been cut back at that time and they felt should be restored - the off-hours.

Q. The one I am most interested in, Doctor, is No. 8.

A. Yes.

Q. And I am quoting:

"That a Pharmacy-based IV and admixture program be established to significantly reduce the potential for medication errors inherent in the present practices."

A. Yes.

Q. And that was with respect to a specific concern I am assuming.

A. Yes. I just can't recollect right now which concern it was that led them to put that in there. They are not - they are talking

rather more I think about the use of some complicated drugs such as those used in cancer chemotherapy rather than sort of routine intravenous drug administration.

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I don't think that they were - even taken out of context it may look like they are suggesting that every antibiotic administration, for instance, ought to be prepared in a central pharmacy. That wasn't the intention at that time.

Q. Well, perhaps to be fair to you I ought to ask you to go to page 8, Doctor.

A. Yes, okay.

Q. Which is the chapter on medication systems.

A. Okay.

Q. And after defining in the first paragarph what a medication system is the report concludes at the end of that paragraph and I quote:

> "The present medication system falls considerably short of these requirements.
>
> The present medication system delivers the drug to the nursing unit, and stops at that point. Not only is the present system restricted to a product delivery system, but to an outmoded delivery system. From our limited observations the following deficiencies

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"exist. Drug orders are filled on the receipt of a transcription from the physician's original order, nurses are required to complete requisitions for ward stocks; drug administration schedules are based on the ancient medication ticket system, and the narcotic control system involves excessive paper handling."

So the recommendation to which I have just referred relates to those general problems described on page 8.

A. Well, you are getting apples and oranges mixed up here.

Q. I am sorry.

A. There is no question that drug delivery system, the system for drug stocking on the wards, was outmoded and required attention. I don't think there is any dispute about that at all. But you are bringing this question of an IV admixture policy which was the one No. 8.

Q. Well --

A. That was the one I think if you go over on page 9 you will read there that they are recommending:

"A pharmacy-based IV admixture program (be developed) which will significantly reduce the potential for medication errors inherent in the present system..."

and that is fine. This is really a unit dose system they are talking about, but it said - they go on to say:

"It should be noted that medical and nursing support for such a service exists on the oncology service."

And this was their area of prime concern. And then they said:

"Such a unit should be considered as a pilot program for a decentralized... service."

I don't think - they were not -- the preparation of IV drugs in the Hospital at that time was not nearly as outmoded as the rest of the drug distribution system. In fact it was very similar to what was in use and is in use in most hospitals in Canada today, so I don't want you to get the impression that they were completely castigating the Hospital for the lack of an IV admixture program.

Q. But to put it this way, the drug distribution system was less than adequate but

within the drug distribution system you are saying the IV admixture system was not so bad?

A. No, the IV admixture program is one small wrinkle in that whole question of drug distribution. It happens to be an area where errors come and they occur so unit dose is likely to produce major benefits. And when they are talking about a centralized IV admixutre service they are really talking about a kind of unit dose system. But I think they were talking here in terms of a constructive recommendation that you should set up a pilot program and see how this works.

Q. Can I take you to the conclusions, Doctor, which are found on page 19, and dealing with the first paragraph:

> "On the basis of the information provided to us through documents and personal interviews, and on the facts and impressions gained through two days of on-site visits, we must conclude that the services of the Pharmacy Department of the Hospital for Sick Children do not meet the needs of the Hospital. In fact, they do not meet the acceptable standards for a modern hospital pharmacy service."

Did you agree with that conclusion at that time, Doctor?

A. Yes.

Q. And since that time am I correct that another study has been done?

A. I am not aware of another study. To what are you referring?

Q. Another report, rather. The report done by Jane Gillespie.

A. Well, I am not sure specifically to what you refer.

Ms. Gillespie is head of the pharmacy now and she presumably reports to the administration on a regular basis on how her department is running.

Q. Well, let me show you one specific report, Doctor, and tell me if you have seen it before and are familiar with it.

A. I don't recall seeing this previously. It doesn't ring any bells just right off.

Q. The report that I am showing you refers to a Jenkinson report which is attached as an appendix. Have you seen the Jenkinson report?

A. No, I don't recall ever seeing

that. It was done prior to my arrival at the Hospital in 1978.

Q. The Jenkinson report was done prior to your arrival but the Gillespie report was done after your arrival.

A. Yes. To me this looks like a report - I am not sure what the purpose of it was, but it was probably a report directly to the administration and as such I don't believe that it was ever considered by the Pharmacy and Therapeutics Committee so I can't help you with that.

Q. Would it be the case then, Doctor, while you have been Chairman of the Pharmacy and Therapeutics Committee that a report about the medication system in the Hospital would not have come to your Committee as a normal course?

A. Oh, yes, that is quite possible. We are not concerned with the day to day operation of the pharmacy. That is the responsibility of the head of Pharmacy, Ms. Gillespie.

Q. Would you not be concerned with the day to day administration of drugs in the Hospital?

A. Not on a day to day basis, no. We are concerned with general policies relating to that.

Certainly we are concerned in a very real sense with the overall operation of the pharmacy and whether it is - whether the systems in place are effective and optimal for patient care, that is why we requested this report by Dinel and Summers. But certainly there is a direct line of reporting from the head of Pharmacy to a responsible administrator that doesn't involve the Pharmacy and Therapeutics Committee.

Q. Did I understand you correctly last week, week before, Doctor, to say that the error rates might be as high as one in two hundred doses administered?

A. I was referring there to the rate of error of one particular kind. That is the wrong drug given to the wrong patient.

Q. Right. And if we can assume for a moment that to be a reasonable error rate --

A. It is not reasonable but it is probably correct.

Q. Factually correct, and if we can assume for the moment that there are on the average 40 children in Wards 4A and 4B at a given time.

A. Yes.

Q. I would ask you to make that assumption. Can you tell me, Doctor, what the average number of medications prescribed to a patient on Wards 4A and 4B would be today?

A. That is a little difficult. It really depends on what you define as a medication, whether you count vitamins, whether you count intravenous fluids and various things.

Q. For the moment --

A. But a ball park figure would be about 10.

Q. 10 today?

A. Yes.

Q. If we had our hypothetical 40 infants or children in 4A and 4B receiving 10 each or a total of 400 per day, there is a possibility per day that two wrong drugs are administered to the wrong patients?

A. Oh, yes. Actually it is worse than that. When I say 10 I am talking about 10 drug entities. Now most of them are given more than once a day so --

Q. So in fact it could be --

A. So we are really talking probably about something like 800 or 1,000 drug

administrations per day on a ward of that size; different drugs to different patients.

Q. So it could be as high as four or five wrong drugs administered to the wrong patient per day?

A. Yes. Either wrong drug or wrong patient. It all amounts to the same thing. That is approximately correct.

Q. And would you agree with me that that isn't the fault of an individual so much as the system which requires the delivery of drugs to the floor in a particular way, recording in a particular way and the administration in a particular way?

A. Well, I think in the end under all of the drug distribution systems - we are getting into semantics here - but of all the systems that are used to assure that the right drug gets to the right patient at the right time there is a final common pathway, and that is the person who administers the drug, and there is a responsibility on that individual to make sure that they are giving the right drug to the right patient no matter what the inadequacies of the system before that point. So I can't agree that that person is totally blameless if they give

the wrong drug to the wrong patient.

Q. Dealing with the issue of who actually administers it, I think Mr. Knazan asked you about the responsibilities of an R.N.A.

Dealing now with just the nurses would you agree with me that nurses do not generally administer IVs, digoxin by IV?

A. No, they generally do not. There is very little use for intravenous digoxin under any circumstances. There certainly are some units where nurses would be cleared to do that.

Q. Was 4A and 4B during this period in question?

A. I can't answer that question. I doubt that it was ever formally written down that that could be done. Certainly in the Intensive Care Unit it was written down. 4A/B, I don't believe that it was formal policy, and probably if ever done, very infrequent and likely with the doctor nearby.

Q. In connection with our hypothetical four to five wrong drug errors per day, would you agree with me most of those go either unnoticed or unrecorded?

A. Oh, yes.

Q. In fact using our hypothetical

of four to five per day would as many as one per day be recorded?

A. No, not at all.

MS. KITELY: Those are all the questions I have, sir.

THE COMMISSIONER: Thank you.

Mr. Shanahan, have you any?

MR. SHANAHAN: No, I have no questions of this witness, thank you very much.

THE COMMISSIONER: Mr. Shinehoft?

MR. SHINEHOFT: I have already cross-examined.

THE COMMISSIONER: Oh, I'm sorry. Oh, yes, you were first I remember.

Well then, Mr. Ortved, did we pass you by?

MR. ORTVED: I think you did but I have no questions, thank you, Mr. Commissioner.

THE COMMISSIONER: All right.

Mr. Roland?

RE-EXAMINATION BY MR. ROLAND:

Q. Dr. MacLeod, picking up on Exhibit 257 which is the review of pharmacy services done in 1980, and turning to page 9 of the conclusions, Miss Kitely has read you the first paragraph, but I

see from the balance of the conclusions that first of all the authors indicate that the attitude of the senior Clinical Department and senior heads and all the members of the nursing service is such that this Hospital has the potential to develop one of the most exciting and advanced pediatric pharmacy services in North America.

It goes on to indicate that the service could be an excellent service if some of the recommendations that are made in this report are implemented, and that because of the costs and the complexity of implementing the recommendations obviously that would be done over a number of years.

Can you tell us, Dr. MacLeod, have these recommendations been implemented or are they in the process of being implemented by the Hospital?

A. Oh, yes, many of the things suggested in this report have been implemented and are in the process of development.

Q. And for instance we have heard that there is a unit dose system with respect to Wards 4A and 4B in the Hospital and that that has been in place for some time.

A. I'm sorry, the unit dose system?

Q. The unit dose system for Wards 4A/4B.

A. It is partially in place I think is more correct to say, but it should be pointed out that in fact at the time of these events from the summer of 1980 through March of 1981 that the Cardiology Ward probably had the best drug distribution system in the Hospital in that they had a full time pharmacist who was assigned to that ward, so many of the problems with drug delivery that are alluded to in this report had already been corrected on that ward.

In fact I see here on page 9 of the report they refer to the planned introduction of an improved medication system on the fourth floor.

Q. Yes.

A. They complained that this perhaps had not had adequate planning, but the fact was that that was introduced in the summer of 1980 just about the time that this report was introduced, and I think it is fair to say that the medication delivery system was greatly superior on that unit than anywhere else in the Hospital.

Q. And can you tell us, Doctor, generally what is your view of the pharmacy and

medication system in the Hospital? Is it meeting the needs of the Hospital?

A. It is infinitely improved. I think we still have some way - and it certainly is meeting the needs of the Hospital on a day to day basis. There is no doubt about that at all.

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I think we still have two or three more years to go in order to achieve nirvana but in part the limitations are the space and facilities available to us and the facilities available to pharmacy are somewhat outmoded.

Q. Are there plans in the works to improve the pharmacy even further in the next two or three years?

A. Oh, yes. We are I suppose on a five-year plan that will culminate in total installation of a unit dose system but for it to be a 100 per cent unit dose system will probably require a new physical plant.

Q. Now, Doctor, dealing with Baby Allana Miller for a moment, you have told us in your evidence, and I think the witnesses have as well, that there is some concern with respect to Baby Allana Miller that the resuscitation efforts with respect to Baby Miller may have somewhat elevated the level of digoxin in her serum or in her blood because of the assault really on her heart at the time of her terminal events to try and resuscitate her.

Let me just ask you briefly again to describe to us how that comes about because, as

I understand it, your evidence is that it is that really assault on that baby's heart, Allana Miller's heart that dislodged the digoxin that was bound both to the ATPase and perhaps non-specifically bound in the heart. Can you tell us in your own opinion with regard to that, which I think you have given, that that would elevate or theoretically elevate the blood serum somewhat, where would that digoxin come from. Is that specifically or non-specifically bound digoxin in your view?

A. Well, at some point I think the question of how it is bound in the myocardium becomes truly irrelevant, that the one thing is absolutely clear and that is that there is a tremendously high concentration of digoxin in the muscle compared to the amount that is circulating in the blood.

Q. Yes.

A. And I think you have heard this repeatedly that there is about a half of one per cent of all digoxin in the bodies in the blood and a larger proportion bound in various tissues including skeletal muscle, skin and so forth.

But the greatest concentration is likely to be in the ventricular muscle.

Q. Yes.

E3 A. When that ventricular muscle is damaged by resuscitation or by some other disease process so that the muscle cells die so that the integrity of the muscle system and the membranes around it is lost then some of that high concentration of digoxin may well be released into the surrounding area and what is in the surrounding area is blood sitting in the ventricular cavity, sitting in the venticle itself, and under these circumstances the concentration of digoxin in that blood may rise, and it may rise even fairly rapidly if there is a rapid destruction of tissue in the immediate vicinity.

Q. And as I understood from your evidence the other day something like 97 per cent of digoxin in the heart is actually non-specifically bound rather than specifically bound to the ATPase

A. Yes. I am not a particular expert on the binding of digoxin to sodium potassium ATPase but at the recent meeting at the hospital people who are more expert than I am suggest that only about 3 per cent of the digoxin is actually bound specifically to the sodium potassium ATPase which means that the other 97 per cent is

non-specifically bound, although may be fairly tightly bound. It isn't bound directly to the so-called receptor.

Q. And that other 97 per cent you say may be tightly bound. Is it thought to be as tightly bound as the ATPase binding?

A. That is a very tough question to answer. One would assume, just extrapolating from the knowledge of biology in general, that it is less tightly bound, that the tightest binding is the very specific receptor, the sodium potassium ATPase. But it may still be very very tightly bound for all practical purposes requiring energy to keep it bound to other protein molecules.

Q. All right. Let's turn a little bit to Baby Cook so that I understand your evidence and particularly your response to Mr. Young this morning.

You gave us in your evidence the earliest time that you felt was possible for a single dose of digoxin, I think a single adult dose of digoxin had been given to Baby Cook to produce the numbers both in the serum and in the tissues and you have put that time at 3:45?

A. Yes.

Q. Approximately. Mr. Young asked

you if there could be for instance in theory then 2 or - I gather he could take it even further, 3 or 4 adult doses possible to produce those numbers given at some earlier stage than 3:45 and you indicated at least with respect to adult doses that that was possible. Do I have that right so far?

A. Yes, that is correct.

Q. All right. Let's take for instance then two adult doses. I gather, first of all, that is a substantial volume for Baby Cook but your view is that that is not sufficient to drown the baby?

A. No, we are talking about 4 millilitres, that's not a huge volume.

Q. Yes, right.It is though I take it a fairly substantial volume to give rapidly to Baby Cook?

A. Yes.

Q. When we take into consideration the propylene glycol effect?

A. Oh, yes. There would be difficulties in giving that rapidly and certainly you run into the potential hazards of propylene glycol.

Q. I gather as you get up to the size of two adult doses you are running into much higher potential of risk from propylene glycol as you get to that kind of level of volume?

A. Oh, yes, certainly that would be true.

Q. So, if that kind of volume or amount of propylene glycol was administered fairly rapidly, you would expect then there would be a very quick reaction to the propylene glycol?

A. Yes. That's not a universal occurrence though, so, I don't think you could - I think you would be running a risk of that if you were giving an intention overdose and hoping to get away.

Q. Yes.

A. But you couldn't assume that this would happen every time. Some people can tolerate, some patients can tolerate very rapid administration of these drugs without any complications at all.

Q. And I take it that the administration you would want, if you were giving that volume therapeutically of propylene glycol, obviously you are giving digoxin, but propylene

glycol I gather is used as a solid for a number of drugs, and let's pick a drug that is given therapeutically and is dissolved in that volume of propylene glycol, that you would want to give that therapeutically over a substantial period of time, something like five minutes or more.

A. Yes, that is correct.

Q. All right. If we go up to three or, say, four, let's take four adult doses, I gather the risk is even greater if you administer that volume of propylene glycol rapidly that you are going to have a reaction to the propylene glycol?

A. Oh, yes. Certainly the risk increases as a dose-related phenomenon.

Q. All right. How high do you have to go before you can say the risk is not only great but it is very probable?

A. Oh, gosh, I'm not sure that you can ever predict the response to this type of chemical. I mean, I suppose there is a dose of propylene glycol that will be universally fatal but I don't know precisely what it is and I'm not sure it has ever been defined even in animal studies.

Q. Let's talk about volume. We have heard about the risk of drowning a baby. Let's take Justin Cook. If given large volumes of intravenous drugs or solutions, what volume would you have to get to before that's a risk?

A. Well, there is a technical problem with just pushing volume into the baby's veins. Cook - do you have his body weight, does anybody recall? I think he was about 3 kilos, was he not?

MR. LAMEK: 5.36.

THE WITNESS: 5.36 kilos. So, this is a good-sized baby. It is not a premature baby. He presumably had reasonably good veins. So, you could probably push in a volume of - before I give you a dogmatic figure I had better think about it. I would think you could push in 6 or 8 ml's without too much difficulty over a couple of minutes.

Q. Yes.

A. If you pushed it in any faster - if you pushed in, say, 8 ml's any faster than that you would disrupt the vein. You probably couldn't push it in as fast - you certainly couldn't push it in as fast as you could into an adult.

As the total volume that he might tolerate before going into heart failure or drowning, as you say, that is a little more difficult. This is a child who already has a compromised cardio-vascular system, so, he can't tolerate the kind of volume that might normally be tolerated, but I would think that, you know, we are talking about maybe 25 ml's there would be the outside volume that he could tolerate over a period of a half an hour.

Q. Can you refresh my memory, how much is the volume of an adult?

A. 2 ml's.

Q. 2 ml's?

A. Yes.

Q. So, you say 25?

A. So, we are talking about a dozen.

Q. A dozen.

A. I mean, it would be physically impossible to give a dozen ampoules of that size, to give 25 ml's quickly, I mean, over a minute. I think you just couldn't do that. But you probably wouldn't drown "drown the baby" with that volume given over a half an hour.

MR. ROLAND: Thank you, those are all the questions I have.

THE COMMISSIONER: NOw, Mr. Lamek, normally we would take a break. Does that seem reasonable?

MR. LAMEK: Sounds perfectly reasonable, Mr. Commissioner.

THE COMMISSIONER: No, I just didn't want to take a break - as I understand it, chances are that we will not have another witness this afternoon.

MR. LAMEK: That's right. We have Dr. Fay for tomorrow morning coming in from Kingston, sir.

THE COMMISSIONER: And you will be finished if we take twenty?

MR. LAMEK: I'll be finished well before.

THE COMMISSIONER: If we take 20 minutes you will still let us get out for lunch?

MR. LAMEK: We're not in any danger of not finishing by lunchtime.

THE COMMISSIONER: All right, we will take 20 minutes.

--- Short Recess.

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--- on resuming.

THE COMMISSIONER: Before we start, I think it is you, Mr. Lamek, I intend tomorrow at the opening of the proceedings to give judgment on that motion under the Public Inquiries Act.

That is all.

Yes, Mr. Lamek.

REDIRECT EXAMINATION BY MR. LAMEK:

Q. Dr. MacLeod, can we start with something that was mentioned in the course of your response to a couple of questions by Mr. Roland a few moments ago on Exhibit 257, the Dinel-Summers Report. I don't know whether you have that.

A. I just gave away my copy. Maybe I can get one back.

Q. You were referring to the page numbered 2 under the heading of "Summary of Recommendations", and it was you, I think, Dr. MacLeod, who drew attention to Recommendation (B)(9):

> "That a multi-disciplinary team be established to plan, implement and evaluate the new medication system proposed for the fourth floor."

Now, this was the study that

F2 apparently had taken place in August of 1980.

A. The report was written -- actually, the two dates on it refer to the days when Drs. Dinel and Summers visited the Hospital. As I recall, they wrote the report on-site, so they probably did write it on the 1st of August.

Q. Can you tell me why a new medication system had been proposed for the fourth floor? Was this some sort of pilot project?

A. Yes. This was really -- the mechanism was in place for establishment of this as a prototype for a ward pharmacist system. Now - I mean, there are many different drug distribution systems -

Q. Yes.

A. One of them, one possible operation is to have a pharmacist on each ward or in each nursing unit, so you have got a central pharmacy and then you have got all these satellite pharmacies, and the pharmacist on that ward looks after the actual maintenance of stock on the ward. She is also there to provide some in-service education for the nursing staff or medical staff and is available as kind of a local expert on drug problems, problems of drug interaction, adverse

F3 drug reaction and so forth.

Q. Yes.

A. And that was the system that had been envisaged by the previous Chief of Pharmacy at the Hospital. The fourth floor, I guess, was to be the initial introduction of a ward pharmacist.

Q. Okay. So the suggestion of this new system on the fourth floor was not something that originated with Dinel and Summers; it was something that had been proposed and they were commenting on the way in which the proposal was to be implemented?

A. That is correct.

Q. And it appears from the top of page 7 and half-way down page 9 that they thought perhaps some more integrated planning involving different disciplines might go into the implementation of that particular proposal?

A. That is correct.

Q. Was there any particular reason for selection of the fourth floor for introduction of this pilot system?

A. I don't recall precisely why the fourth floor was chosen. Partly because the

F4 floor had recently been renovated and so there were better facilities available for drug storage and development of something of a satellite pharmacy on that ward, I believe.

The other consideration would be that drug therapy is complicated in cardiology patients and this would be an area where a ward pharmacist would be particularly useful.

Q. We know that a ward pharmacist was introduced into the cardiology wards.

Do you recall the date of that, Dr. MacLeod? I'm afraid I don't.

A. No. I believe she started in August of 1980. It may have been September, but it was about to start at the time that Dinel and Summers visited.

Q. And was that a development that was welcomed by the nursing staff on the floor?

A. To the best of my knowledge, but I don't recall ever specifically discussing it with the nurses on that floor.

Q. I take it that the hoped for result of the introduction of this new system would be a reduction in the incidence of medication errors?

A. That would be one of the

F5

objectives, but a somewhat indirect objective.

If you have a good system operating with an on-site pharmacist and continuing education of nurses and doctors and other staff on the ward, then you hope - and some rationalization of the drug distribution system, the maintenance of inventory on the ward - you hope that in the long run that will translate into fewer medication errors. But if somebody had said, is that the direct objective, the answer would be, no.

Q. It would be one of them?

A. It is an indirect benefit, if anything.

Q. Were any studies done to establish the incidence of medication errors after the introduction of the new medication system on the fourth floor?

A. I am not absolutely certain that it is fair to call it the establishment of a new medication system. It was the introduction of a ward pharmacist and perhaps a more pharmacy-oriented way of maintaining inventories on that ward. But as to whether or not there was a study of medication errors, not to my knowledge. We have always had a system of reporting medication

F6

errors, which is a voluntary reporting system, as you probably heard.

Q. Yes.

A. And subject to all the limitations of that system.

Q. Including the fact that a person who has committed an error may not be aware that it has been committed?

A. Oh, absolutely. That is probably the norm in fact.

Q. Just with respect to drug errors, Dr. MacLeod, I was interested in your evidence about the possible or likely incidence of errors involving confusion of drugs and/or patients which you say are both sides of the same coin.

Is there any study of which you are aware, or do you have any opinion as to whether there is a greater propensity to confuse drugs and/or patients with respect to, for example, vitamins than with respect to known dangerous drugs such as digoxin?

A. I don't know. It is an interesting question but I don't know of any study that has been directed specifically to that question.

Q. Another particular kind of

F7

medication error that has been suggested, which you address both in your evidence in chief and in cross-examination. This is the possibility that the syringe that was taped to Justin Cook's bed may have indeed contained not inderal, as was thought, but digoxin.

Do you recall the various questions about that?

A. Yes, I do.

Q. Can I ask you first whether 0.6 milligrams of digoxin, millilitres of digoxin, administered at about 3:45 in the morning would, in your opinion, have produced the levels found in the serum and fresh tissue of that child?

A. Well .6 ml. we are talking about 130 micrograms of digoxin, assuming it was an adult strength digoxin.

Q. Yes.

A. No, I don't. I think it would be at the outer limits of the possibility but very much at the outer limits.

THE COMMISSIONER: You mean that would not have produced a higher reading?

THE WITNESS: I don't think it would be -- the question was administered at 3:45, would it

F8

be adequate to produce those levels of 1,100 nanograms or more in tissue.

MR. LAMEK: Q. Fresh tissue, yes.

A. All things are possible, but I think this really is at the fringe of possibility.

Q. Because it seems that the candidacy of that particular drug error rather rested upon the timing of the administration of the inderal, did it not?

A. Yes.

Q. At about 3:45, which coincides with your best view as to the most likely time of the administration of digoxin to produce those levels.

A. The only reason I hesitate at all is because of the point I made ten days ago; that is, we just don't absolutely know what happens after an administration of intravenous digoxin. It is remotely possible that you get an initial very high concentration in tissue and then it falls off equally quickly to give us the kinds of concentrations that are normally measured in the studies that address that question. So, unless that happens, then it becomes, I think, very unlikely that .6 ml. of digoxin solution at 3:45 would give you that concentration.

F9

Q. Dealing, however, with the possibility, no matter how remote you may consider it to be, Dr. MacLeod, you have said also that you don't think that confusion would be likely between vials of digoxin and inderal, again recognizing that too is possible?

A. Yes.

Q. And you have also said that it is your better judgment that digoxin was probably deliberately administered to Justin Cook?

A. Yes.

Q. Now, if those be your beliefs, Dr. MacLeod, and if digoxin were administered instead of inderal at 3:45 in the morning, is it also within contemplation that that confusion may have been deliberately engineered?

A. Yes, I think so.

Q. That is to say, that as between the vials of inderal and digoxin, the likelihood of confusion is small but that it is possible that someone may have deliberately taped to Justin Cook's bed the syringe which everybody believed to contain inderal but which, in fact, contained digoxin and which was administered about 3:45 in the morning.

F10

A. Yes, I think that is a possibility.

THE COMMISSIONER: Although investigations did not include investigation of the syringe but they did all those tests?

MR. LAMEK: I'm sorry?

THE COMMISSIONER: All the tests, they did the test of the IV bag and everything else but they never did a test of the syringe.

MR. LAMEK: I think not, Mr. Commissioner. I am not aware of one.

—

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THE WITNESS: I think the syringe - no, I don't recall that there was ever a test of that syringe. I am not sure that it was available. It may have been thrown out with the various garbage from the room.

THE COMMISSIONER: I thought they were most keen at that particular point to test everything they could.

THE WITNESS: Well they did test the intravenous fluid at that time.

THE COMMISSIONER: These syringes, they are reuseable, are they not?

THE WITNESS: No, they are all disposable now so it would have just been dropped in the garbage after being used.

THE COMMISSIONER: As soon as it was administered it would go in the garbage.

THE WITNESS: Yes.

THE COMMISSIONER: And probably would have been disposed of before the child died?

THE WITNESS: Oh, might well have, yes.

MR. LAMEK: Q. Could we add a piece of information to the picture, though, Dr. MacLeod? It appears from the chart it was

G2

Dr. Kantak who was called to see Justin Cook at 3:45 in the morning when the Inderal was administered and he gave evidence at the preliminary hearing - his evidence, Mr. Commissioner, is found at Volume 25(II) at page 26, question - which I should probably start at the very foot of page 25, question of Dr. Kantak:

"Q. In any event, you went to bed I understand in the early hours of the morning you were called, Dr. Kantak.

A. Yes. Around 2, 3 o'clock I was called and the nurse informed me that the baby was blue and was in bad shape.

Q. Which nurse was that? Do you know?

A. They called me. I don't know.

Q. You were on the floor, on the fourth floor?

A. Yes, sir."

Page 26:

"I walked off from the room up to the ward, saw the baby. The baby indeed had turned very ill. I examined the baby and he did not have any murmur. I realized the baby had a tet spell,

G3

"so I gave the baby intravenous propranolol. I don't know the exact amount, but it would be somewhere around .1 to .2 milligrams per kilo of the dose."

He repeats that:

"A. We had specific...we had calculated the amount and capped it.

Q. Yes. Okay?

A. So I gave him intravenously that medication, intravenous propranolol, which I took from the foot end of the bed again, and there was a vial of Inderal, of propranolol attached to a syringe.

Q. Now had you drawn that up earlier?

A. No, I didn't draw it. It was drawn earlier because the order suggested it should be drawn and attached to the foot end of the bed.

Q. Did you see it being drawn?

A. No, sir.

Q. But it was drawn up and attached to the bed earlier?

A. Yes, sir."

It appears from that evidence of Dr. Kantak who actually administered the propranolol but there was not merely a syringe with propranolol but attached to it a vial of propranolol or a propranolol vial which I take it would be presumably to identify the contents of the syringe.

A. Yes.

Q. Now, Doctor, can we address the significance of that for a moment, please?

If as Dr. Kantak said under oath an Inderal vial was attached to the syringe, would you agree that that means - I can think of three possibilities and I ask you to consider them with me and add any others if you can - it may mean first that somebody was so studiedly and conscientiously careless, if I can put it that way, as to go to the trouble of attaching an Inderal vial presumably for identification purposes to a syringe of digoxin which just happened to be lying around - that would be extraordinary bad luck, would it not?

A. I would agree.

Q. And would you agree that that is a highly unlikely scenario?

A. Yes. I can't imagine that.

Q. A second possibility I suggest,

Doctor, is that someone deliberately substituted a syringe of digoxin for a syringe of Inderal and equally deliberately attached an Inderal vial to that syringe for the purpose of misleading as to the contents.

Is that a second possibility?

A. Yes, I think that is possible.

Q. Right. And the only other one that occurs to me, Doctor, is that the sryinge at the bedside did indeed contain Inderal as the attached vial suggested, and that the use of the syringe was not the occasion of the administration of digoxin. Is that also a possibility?

A. Yes, I think that is possible too.

Q. And indeed in light of what you have said, Doctor, about the remote likelihood that the administration of .6 milligrams of digoxin at 3:45 --

A. .6 ml.

Q. .6 ml of digoxin at 3:45 producing the levels that were found in Cook is the third not the most likely possibility that the syringe did indeed contain as advertised Inderal?

A. Yes, that is I think the most likely.

I have just been looking at the chart here, though, and listening to what you were reading from at the preliminary hearing, and we shouldn't be tied too much I think to that value of .6 ml.

Q. Yes.

A. It is clear that that is the ball park figure. Dr. Kantak says .1 to .2 mls per kilo which really puts it between .5 and 1 ml on the first occasion.

Q. Yes.

A. And then there is the second dose as well.

Q. The chart says .4 then .2, Doctor.

A. There is a note here written by Mounstephen.

Q. Yes.

A. Which is really the account of the arrest which was probably after the fact but does start at the very top of the page as Inderal .4 plus .2 equals .6 ml. I don't know really which - we are not talking about a large volume I think.

Q. Indeed if the note, and I have to tell you, Doctor, it was not written by

Dr. Mounstephen but signed by him, be correct --

A. Yes.

Q. A total of .6, that is the number I have been putting to you.

A. Yes.

Q. It was on that basis that you considered the possibility of that volume of digoxin unlikely to produce the result seen?

A. That is correct.

Q. If indeed Dr. Kantak's evidence is to be preferred it is an even smaller volume, is it not?

A. No, no, he is talking about a larger volume.

Q. Oh, I'm sorry.

A. He is talking about - there are two administrations.

Q. Yes.

A. The first one he said .1 to .2 mls per kilo.

Q. He is a doing it by weight, that is right.

A. Yes. Multiply by 5. He is talking about .5 to 1 ml given in the first instance and then a supplementary dose given again, so then

you are getting up to a larger volume and, you know, the question of how much digoxin would have been given if there was a mixup in those, in the syringe --

Q. Sure.

A. -- you know, changes.

Q. Can we just address for a moment the question of the post mortem multiplier about which we have heard so much over the last few months and about which you have spoken.

You referred in particular to the case of Gary Murphy who you said showed something like a multiplier of 14 times. Indeed of the information we have, Doctor, the multiplier appears to be rather more in the range of 21 and perhaps you should be looking at Exhibit 232.

Could the Registrar give you that, please?

A. Yes, I think it depends on which of the post mortem serum values you take.

Q. That is right.

A. To compare the 1.8 ante mortem. I guess you are taking the value of --

Q. 32.2.

A. Even that wouldn't give you 21 I am sure. I don't have my calculator here.

Q. The ante mortem level was 1.5.

G2

EMT:
yk

A. Okay. I am taking 1.8 as the ante mortem. Is that not correct?

Q. Well, isn't the truth of it, Dr. MacLeod, that we don't really have an ante mortem level with which to compare the post mortem level?

A. Yes, I think that is absolutely correct in the case of Murphy, and I think I made this point ---

Q. The ante mortem level that we have is some 19 days prior to death.

A. So it is not a very good case on which to make this relationship.

Q. It is indeed fairly, is it not, impossible to make a relationship with a level that far in advance of death?

A. Yes, I think so.

Q. Especially on the theory put to us by Dr. Spielberg which you have acknowledged you consider to have validity that the progressive necrosis that was occurring in the tissues of this child may well have produced a continuing unbinding of digoxin in the last days of his life?

A. Yes.

2-2

Q. If that be so his immediate ante mortem serum level may have been very considerably higher than that recorded 19 days earlier?

A. And my guess is that it was.

Q. Yes. And therefore if we are looking for the outer ranges of a multiplier I suggest to you that Gary Murphy doesn't really give us any guidance at all, does he?

A. No, I really think we should ignore it. It really represents one extreme, but in fact the basic fallacy that you have just elaborated in the Murphy case is there in much of the other data that is in the literature. The ante mortem levels are taken at variable times before death and may or may not bear any reasonable relationship to the post mortem concentration.

Q. Because indeed as we know all sorts of things can occur during life, particularly in a very sick child, which may affect the serum level of digoxin?

A. Absolutely.

Q. There may be renal failure to some degree or another; there may be the kind of unbinding that occurs from progressive necrosis of tissue and so on.

2-3

A. Certainly there are many agonal events that undoubtedly put the digoxin up even before the actual moment of death.

Q. Sure.

A. I think this is the point you are making.

Q. And it may be a progressive situation?

A. Yes.

Q. In terms of the progressive elevation of digoxin level in the last days of life.

A. Yes. Certainly we have evidence that that happens.

Q. Indeed looking at the whole of the numbers that are in Exhibit 232, and you have referred I think to that study by Dr. Phillips to establish a range of multipliers recorded, it is the case, is it not, that in I think of the 37 cases shown there and I believe 23 of them, the ante mortem levels referred to were taken 12 hours or more prior to death. Indeed in many cases a number of days prior to death?

A. Yes.

Q. I take it therefore that in those cases one cannot with confidence rely upon

the multiplier between the post mortem and the last ante mortem sample?

A. No, I think you would have to look at them individually and the nature of their aganol events before you put too much interpretation on them.

Q. And indeed in 11 of the 37 cases there is no ante mortem level available at all?

A. That is correct.

Q. If my numbers be correct, Dr. MacLeod, is it not the case that indeed in only three of the cases is the post mortem level compared with an ante mortem level drawn within 12 hours of death?

A. I would have to look at the chart in detail ---

Q. I ask you to accept --

A. That is a rarity, certainly.

Q. And in those three cases the multiplier it apparently appears is of the order that we have been accustomed to seeing in the literature, 2 to 3 times?

A. I think that is the kind of figure that you should accept as a ball park figure.

2-5

Q. Thank you. So although on the face of it those numbers may appear to suggest multipliers of up to 8, 9, 10 times, even disregarding Murphy, if one looks only at those cases where the ante mortem level is shortly before death, within 12 hours of it, the multiplier that we see is of the order reported generally in the literature of 2 to 3 times?

H:
BM:
yk

A. Yes. I think the only time in which you should seriously consider a greater multiplier would be in cases like Murphy where there was just so much going on that may indirectly elevate digoxin, but that is a very special rare case.

Q. Yes. Doctor, although we have heard that this multiplier effect in digoxin levels after death is a very common occurrence, I thought I heard you say in the context of dealing with Pacsai that there is a universal multiplier effect after death.

THE COMMISSIONER: Universal - it is universal but it is not ...

MR. LAMEK: Not uniform.

THE COMMISSIONER: Not uniform, yes.

THE WITNESS: Not uniform. But it is essentially universal. I think in all of the literature that I have looked at and in all of our samples from the hospital, or virtually all of them there is an increase post mortem.

Q. Okay. In some cases a very small increase, in other cases we will say 2, 3, perhaps even 4 times?

A. Yes, that is correct.

h-2

Q. Just on the question of that multiplier for a moment, Dr. MacLeod. Are there any data to support the proposition that I'm going to put to you - perhaps I should put it in the form of a question. Is it logical to think that the higher the ante mortem level the less will be the effect of the post mortem multiplier?

A. Well, I think we've gone over this ground before.

Q. Yes.

A. That's an assumption that I would make and it is a testable hypothesis.

Q. Sure.

A. But it is not something that you can prove from the literature.

Q. If your hypothesis be correct that one of the causes or a major cause or perhaps the only cause of the elevation in serum post mortem is the release of digoxin from tissue, then would I take it that the amount of digoxin released from tissue is a function of what is in tissue rather than what is in serum?

A. Yes, that is correct.

Q. And if that be so, and if a serum level representing therapeutic loading of let

h-3

us say 2 nanograms may be increased by 2, 3, perhaps fourfold after death, that tells us something about the amount of digoxin that's been released, does it not?

A. Yes, that is correct.

Q. However the ante morten level is 70, 80, 100, to achieve a multiplier of 2, 3 or 4 there, there would have to be a vastly greater amount of digoxin released from tissue post mortem?

A. Yes, that is correct.

Q. And is there any evidence to suggest that the amount of digoxin released post mortem from tissue went into serum is influenced by the amount of digoxin in serum at that time?

A. No. Well, this I think is the question we started out with at the beginning of our testimony.

Q. Yes.

A. There really is no direct evidence of that. One likes to assume that there is something of an equilibrium established and that may not be correct. I mean, if you take a child like Justin Cook, if there is a concentration of 1100-plus nanograms per gram of tissue and if one gram of that tissue, which is immediately

adjacent to the ventricular cavity, just completely necrose, breaks down, releases that digoxin, you have now got an extra 1100 nanograms that is available to equilibriate with the fluids that are sitting in the ventricular cavity. Obviously that can produce a considerable artefact.

Q. Sure.

A. Considerable artefact. So, whether it is a true equilibration in the chemical sense or whether it is just a local phenomenon as tissues break down and disgorge their digoxin into the adjacent fluid, serum, but whatever it is, I don't know, but I think there is certainly potential for that happening.

Q. Well, the matter occurred to me in the context of your discussion of Kristin Inwood with Mr. Labow this morning. The 1100 nanograms in the Cook's heart tissue will be there presumably whether at that moment he has 2 or 200 nanograms in his serum?

A. Absolutely.

Q. Okay. With the case of Inwood, is it necessarily appropriate to apply the normal multiplier of 2, 3 or 4 to the level of 491 in order to get back to the ante mortem level. That was

really the question that occurred to me this morning with respect to Inwood.

A. Yes. No, I think you would do that with less certainty than you would in the other cases. In fact, you know, it is possible if that is a bona fide concentration that the movement is the other way.

Q. And indeed at concentrations of that order in post mortem serum the ante mortem serum level may have been higher, you are suggesting, that is possible if equilibriation is playing the part here?

A. Well, the ante mortems may have been higher, yes, that is correct, and with movement into the adjacent tissues, yes.

Q. Or they may not have been appreciably lower?

A. They are certainly not necessarily appreciably lower, that is correct.

Q. My only point is that one cannot assume that with a post mortem level of that order one can automatically say apply the usual range of multipliers to work back to an ante mortem level?

A. No, no, I think you are quite

right in that. You know, we are dealing with a very uncertain science to begin with and a very broad range of multipliers.

Q. Sure.

A. But I did suggest that when you look at Inwood maybe the multiplier is in fact .25, not 3 or 4.

MR. LAMEK: Dr. MacLeod, thank you very much indeed.

THE COMMISSIONER: Yes, thank you, Doctor. That brings the proceedings to an end, does it, for today?

MR. LAMEK: It does until we hear from Dr. Fay in the morning, Mr. Commissioner.

THE COMMISSIONER: All right. Well then, until 10 o'clock tomorrow and, as I indicated, I will give judgment on the Public Inquiries Act, Section 5 at that time.

---Whereupon the hearing adjourned at 12:25 p.m. until Tuesday, November 22nd, 1983 at 10:00 a.m.